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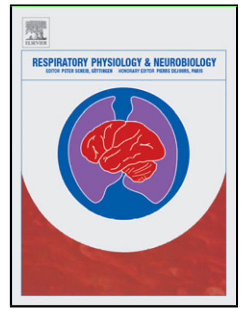

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MUSCLE ACTIVATION AND SOUND DURING VOLUNTARY SINGLE COUGHS AND COUGH PEALS IN HEALTHY VOLUNTEERS: INSIGHTS INTO COUGH INTENSITY

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HIGHLIGHTS

- Very few studies have addressed the influence of cough effort and operating volume on the mechanics of coughing
- In healthy subjects, effort and operating volume have important influences on cough mechanics but modulate muscle activation, pressures and sound amplitude and energy differently.
- Consequently, these cough sound parameters poorly represent cough mechanics and have limited potential as a surrogate intensity measure.

ABSTRACT *(159 words)*

Very few studies have addressed how coughing varies in intensity. We assessed the influence of cough effort and operating volume on the mechanics of coughing using respiratory muscle surface electromyography (EMG), oesophageal/gastric pressures and cough sounds recorded from 15 healthy subjects [8 female, median age 30(IQR 30-50)years] performing 120 voluntary coughs from controlled operating volume/effort and three cough peals. For single coughs, low operating volumes and high efforts were associated with the highest EMG activity ($p<0.001$); the resultant pressures increased with effort but volume had little influence. In contrast, cough sounds increased with both volume and effort. During cough peals, EMG fell initially, increasing towards the end of peals, pressures remained stable and sound parameters fell steadily to the end of the peal.

In conclusion, effort and operating volume have important influences on cough mechanics but modulate muscle activation, pressure and cough sound amplitude and energy differently. Consequently, these cough sound parameters poorly represent voluntary cough mechanics and have limited potential as a surrogate intensity measure.

Key words: Electromyography; Cough acoustics; Intensity.

1

2 INTRODUCTION

The study of cough has, until recently, been hampered by the lack of validated measures reflecting cough severity (1-3). Many factors impact how patients perceive the severity of coughing including how frequently they cough, disruption to normal activities, and the cough intensity, described by patients as the harshness or physical discomfort of coughing (4). Although recently developed quality of life scores reflect disruption to normal activities (5, 6) and objective monitoring of cough frequency is in use in clinical trials (7-9), very few studies have addressed how coughing may vary in its intensity and how this might best be quantified. Indeed there is no agreed definition of cough intensity. High intensity coughing is important as it is likely to be associated with physical complications which may include dizziness, chest pain, vomiting, syncope and incontinence. Equally low intensity coughing may be less distressing but could suggest impaired cough effectiveness.

Cough is initiated by contraction and shortening of the expiratory muscles against a closed glottis, developing high intra-thoracic and intra-abdominal pressures prior to a sudden glottal opening resulting in rapid air flow from the lungs. The flow generated during coughing depends on a number of factors including the volume of air in the lungs prior to the cough (operating volume) (10), the muscular effort applied to this volume and its translation into the driving force necessary for effective cough. Cough sounds arise as a result of this flow and vibration of the tissues of the respiratory tract.

The intensity of a cough perceived by a patient is likely to be related to a number of attributes; intuitively the magnitude of the muscle activation might be expected to be most important, but the resulting pressure and flow might play a role. Investigating the relationships between these measures and how they are modulated by cough effort and operating volume, may enable a better understanding of how cough intensity may vary. It is clearly impractical to directly determine most of these parameters during spontaneous coughing, so we have also studied the cough sound, which is easily recorded and its nature determined by the flow generated as a consequence of the muscle activation and pressures developed.

Previous studies have investigated muscle activation during coughing using surface abdominal electromyography (11, 12), whilst others have studied flow and pressure only (13), but none have explored or controlled for the effects of cough operating volume or the effort applied when coughing. In one study, subjects were trained to produce voluntary coughs at specific flow rates irrespective of operating volume or effort (14). Chest and abdominal EMG signals were recorded and increased with the targeted cough flow but as all coughs followed a deep inspiration, low operating volume coughs were not studied which may not well represent all spontaneous coughing. Moreover previous studies have focussed on single coughs, an uncommon pattern in spontaneous coughing in our experience of recording cough sounds in ambulatory patients. Even in studies that have evoked peals of coughing, the analysis has been limited to the first cough of the peal, disregarding the subsequent coughs (13). During a cough peal, consecutive coughs occur from reducing operating volumes which could conceivably range from total lung capacity TLC down to below FRC, supporting the approach of studying single coughs from different operating volumes and including cough peals.

A few authors have also investigated cough sound intensity which, as expected, is correlated with the flow responsible for generating the sound (13, 15). Cough effort has also been shown to influence cough sounds (16, 17) but again the impact of cough operating volume was not taken into account in these studies and low operating volume coughs, where flow is severely restricted, were not included. Studies exploring the relationships between cough sounds and measures of EMG are lacking.

We hypothesised that the key factors capable of modulating cough intensity were the volume inspired prior to coughing (operating volume) and the level of effort applied. Therefore we explored how respiratory muscle EMG during coughing was modulated by the effort applied during each cough and the cough operating volume. We then related these signals to the pressures and cough sounds produced. We predicted that both cough effort and operating volume would significantly influence muscle activation, pressure flow and therefore the cough sounds. We also compared single coughs and cough peals.

3 METHODS

3.1 Subjects

Fifteen healthy participants were studied. All were non-smokers, had normal spirometry and no history of respiratory infection during the previous 4 weeks. Ethical approval was granted by the local research ethics committee (Kings College Hospital, no: LREC 02-120) and written informed consent obtained from all subjects.

3.2 Protocol

All procedures were performed in a quiet room with the subject seated. A total of 120 single voluntary coughs were completed by each subject. Coughs were performed from four different operating volumes (10%, 30%, 60% or 90% of forced vital capacity (FVC)) and with three different levels of effort (low, medium and high); ten coughs were performed for each condition. Single coughs were followed by three cough peals. During coughs, audio, electromyography and pressure were simultaneously recorded (online supplement Figure E1). Surface EMG electrodes were placed over the abdomen and chest, and catheters were inserted per nasally to measure oesophageal pressure (Poes) and gastric pressure (Pgas)

Audio recordings were made using a piezo-electric contact microphone placed below the suprasternal notch (online supplement Figure E2).

3.2.1 Single voluntary coughs with controlled operating volume and effort

Cough operating volume was controlled using a custom-designed system consisting of a spirometer (Vitalograph Ltd, Buckingham, England) interfaced to a laptop computer via an analogue to digital converter (USB1608 FS, Measurement Computing Corporation, Norton, MA). Interface control and data management were accomplished using custom-written software (Visual basic 6, Microsoft Corporation, Redmond, WA). Firstly the subjects' FVC was determined from the best of three measures in accordance with ATS/ERS criteria (18) (online supplement Figure E3 A). The required cough operating volume was then entered into the software as a percentage of FVC. Subjects, wearing a nose clip, were instructed to take a full breath in (to TLC), and then to breathe out into the spirometer mouthpiece until the target operating volume was reached. The volume expired into the spirometer and target operating volumes were displayed on a screen from the onset of the manoeuvre (online supplement Figure E3 B), and when target volume was reached a loud beep and a visible message 'cough' appeared. At this point the subject stopped breathing out and the mouthpiece and nose clip were removed by a researcher prior to the cough, ensuring the cough sound was not distorted by the mouthpiece/nose clip and that non-cough EMG artefact was minimized. Subjects then coughed with the prescribed level of effort, without taking any further breath in or out. For high effort coughs, subjects were asked to cough as strongly as possible, for low effort to perform gentle coughs and medium coughs intermediate between high and low. Each subject practiced the procedure several times prior to data collection. Careful observation ensured that subjects followed operator instructions.

3.2.2 Voluntary cough peals

The subjects were allowed to rest briefly before performing 3 voluntary cough peals. Subjects were then instructed to take a full breath in and produce a series of coughs for as long as they were able to do so, without breathing in or out between coughs. The subjects remained seated throughout and did not wear a nose clip. This process was repeated three times for each subject. Careful observation of the subjects ensured that breaths were not taken between coughs.

4 DATA ACQUISITION

All data was acquired using an analogue-to-digital converter (Powerlab, AD Instruments, Inc. Colorado Springs, CO) and a computer running Chart 5 software (AD instruments). The software controlled the synchronisation, acquisition and display of EMG, pressure and sound data.

4.1 EMG Measurement

The EMG signals were amplified and bandpass filtered between 10Hz and 3kHz (RA-8 biomedical amplifier, Yinghui Medical Tech Ltd, Guangzhou, China) and acquired and displayed on a laptop computer (MacBook, Apple Computer Corp, Cupertino, CA, USA) running Chart software (Chart Version 5.4 ADInstruments, Colorado Springs/CO, USA) with analog to digital sampling of 10kHz (Powerlab, ADInstruments, Colorado Springs/CO, USA).

The skin surface was prepared using alcohol rub and Neuroline gel (Ambu, MD, USA). Ag-AgCl surface EMG electrodes were positioned on the right side of the body over the parasternal intercostal muscles (second intercostal space, 3cm from centre of sternum, reference anterior shoulder), lateral chest muscles (8th intercostal space in the mid-axillary line, reference 5cm lateral on the 10th rib), lateral abdominals (5cm directly below the costal margin on a line drawn down to the anterior superior iliac spine, reference placed 5 cm medially) and medial abdominals (5cm lateral to the umbilicus with the reference a further 5 cm laterally) see online supplement Figure E4.

Muscle groups rather than single muscles are named as with surface electrode recordings as it is likely the EMG signal acquired arises from several overlying muscles in a group rather than a single muscle.

4.2 Measurement of Gastric and Oesophageal Pressure

Gastric (Pga) and oesophageal pressure (Poes) were measured using balloon catheters (CooperSurgical, Trumbull, CT, USA) inserted nasally (online supplement Figure E4). The catheters and a pneumotachograph were attached to individual pressure transducers (MP45; Validyne, Northridge, CA, USA) and the balloon position established by standard methods (Baydur *et al.*, 1982). The transducer signals were amplified (CD-280 amplifier; Validyne) and acquired at 10kHz using an analogue-to-digital converter (Powerlab; ADinstruments, Chalgrove, UK) and a computer running Chart 5 software (ADinstruments).

4.3 Measurement of Sound

Sound was recorded using a contact microphone insensitive to ambient sounds (Andromed Inc., Saint-Laurent, QC, CA), placed over the manubrium sterni, just below the suprasternal notch (online supplement Figure E2). Simultaneous free field recordings were also made for validation purposes.

5 SIGNAL ANALYSIS

Signal data was saved to computer hard disk for subsequent analysis using custom written MATLAB software (The MathWorks Inc., DriveNatick, MA**)**. EMG signals for each voluntary cough were rectified, and the root mean square value of the signal calculated using a 50ms window. For each voluntary cough and each muscle group the maximum value

(EMG_{MAX}) and the area under the curve of the root mean square EMG trace (EMG_{AUC}) were determined. A graphical representation of these parameters is shown in Figure 1.

5.1 *Single voluntary coughs:*

The start and end of the cough EMG were determined from a window technique based upon the gastric pressure, for detailed description see online supplement. EMG data were normalised by dividing each parameter by the median value of 10 measures from coughs taken from the highest volume and effort coughs i.e. from 90% of FVC with high effort. The maximum gastric and oesophageal pressures ($Pgas_{MAX}$ and $Poes_{MAX}$ respectively) were determined as the peak pressure occurring between the start and end of EMG activity. The start and end of the cough sound were identified using a thresholding technique based on the sound recording background level. Sound parameter ($sound_{AUC}$) takes into account the magnitude and duration of the cough sound. The cough sound was initially high pass filtered to minimise the vocal component of the cough sound (see figures E10 and E11). The AUC envelope was then extracted from the modulus of the high pass filtered cough sound by low pass filtering (see figure E12). .

5.2 *Voluntary cough peals:*

Only the first cough peal was analysed for each individual as data from subsequent peals showed evidence of participant fatigue. The start and end of the cough EMG were identified from the local minima in gastric pressure associated with each cough sound. The parameters previously described for single coughs were calculated automatically for each cough in a peal using MATLAB development software (The MathWorks Inc., DriveNatick, MA).

6 STATISTICAL ANALYSIS

Data were analyzed using SPSS version 19.0 software (SPSS, Chicago, IL, USA). The analysis assessed the influence of volume and effort level on the cough parameters measured. Analyses also explored the relationships between cough parameters during cough peals.

6.1 Single voluntary coughs

General estimating equations were used to assess the influences of cough effort and operating volume on each parameter measured. Data are presented as model means (95% confidence intervals). Using within-subject correlations as described by Bland and Altman (19), we explored the relationships between EMG, sound and pressure, with data stratified by firstly the operating volumes and then by effort level. Data are presented as correlation coefficients.

6.2 Voluntary cough peals

We wished to understand how each parameter changed throughout the cough peals and therefore studied sequential sections. We again used within subject correlations applied to coughs 1 to 6 (the shortest cough peal contained 6 coughs), then 6 to11 (the median number of coughs per peal). Although peals ranged up to a maximum of 23 coughs, we limited the analysis up to the median number to ensure that each analysis included sufficient numbers of coughs. For each section we determined the correlations between each parameter and the cough number.

We also used within subject correlations to explore the relationships between EMG, sound and pressure during cough peals over all 11 coughs, using only the first 6 coughs and then between coughs 6 and 11.

7 RESULTS

7.1 Single Voluntary Coughs

Changes in EMG, pressure and sound parameters with varying effort levels are illustrated for each of the fixed operating volumes studied Figures 2,3, and 4 respectively. Alternative illustrations showing changes in these parameters with varying operating volumes at each effort level studied are available in the online supplement (online supplement Figure E6, E7 and E8).

7.1.1 Surface EMG

EMG signals recorded over the parasternal intercostal muscles were excluded from analysis due to ECG contamination, but for all other muscle groups the influence of cough effort and operating volume are displayed in Figure 2A-F. Both EMG_{MAX} and EMG_{AUC} increase significantly with increasing cough effort, for all muscle groups ($p<0.001$ in all cases). However for operating volume, EMG parameters were most likely to fall as operating volume increased and there was a significant interaction between cough effort and operating volume when predicting some EMG parameters i.e. the effect of operating volume was different at the different effort levels, see online supplement Figure E6. For example, for high effort coughs the medial abdominals EMG tended to increase for coughs taken from 90% FVC (Figure E6 A and B) compared with lower volumes. Conversely, for low and medium effort coughs, EMG_{AUC} was more likely to decrease as operating volume increased (Figure E6 A, C and E). EMG_{MAX} displayed the same pattern for low effort coughs, with medium effort coughs exhibiting a U-shaped curve, for all muscle groups (Figure E6 B, D and F).

7.1.2 Pressure

The effects of cough effort and cough operating volume on pressure are illustrated in Figure 3A and B. Increasing cough effort resulted in increasing maximum gastric (A) and oesophageal pressures (B) regardless of the cough operating volume ($p<0.001$ in all cases).

However, again there was a significant interaction effect between cough effort and operating volume ($p<0.001$) such that at high effort pressure tended to increase with operating volume, at medium effort there was no change and at low effort, pressure tended to decrease with operating volume (Figure E7A and B online supplement).

7.1.3 Cough Sound

The effects of changing effort and operating volume on the cough sound are illustrated in Figure 4A and B. $Sound_{AUC}$ increased significantly with increasing cough effort for all operating volumes ($p<0.003$). There was also a significant interaction effect ($p<0.001$) between cough effort and operating volume for the $sound_{AUC}$ as the effect of effort on $sound_{AUC}$ was greater greatest at higher operating volumes (online supplement Figure E8A and B).

Cough $sound_{MAX}$ behaved similarly to $sound_{AUC}$ for low and medium effort coughs, increasing with effort and operating volumes. High effort coughs had significantly greater $sound_{MAX}$ than medium or low effort coughs, but did exhibit much greater variability. $Sound_{MAX}$ also had a tendency to increase with operating volume.(figure E8B).

7.2 Voluntary Cough Peals

7.2.1 Changes in EMG and pressure with increasing cough number.

When only the first six coughs in each peal were analysed there were moderate negative correlations between cough number in peal and EMG_{AUC} for the lateral abdominals and lateral chest but not for the median abdominals (Table 1). In contrast, there were no meaningful correlations between EMG_{MAX} and cough peal number. Parameters for the first 6 coughs (estimated from the GEE model) are shown in Figure 5, illustrating that although EMG_{AUC} initially falls, as the peal progresses values plateau and even start to increase. Figure

6 shows an individual example of this phenomenon which is underestimated in the analysis of grouped data due to the variable length of the cough peals.

Repeating the analysis using coughs 6 to 11 produced weak negative correlations in EMG_{MAX} for all muscle groups but not EMG_{AUC}. When all 11 coughs were combined in the analysis, the overall effect was that as cough peal number increased (i.e. reducing operating volumes) EMG decreased for all muscle groups and parameters.

7.2.2 Pressure

For the first six coughs in each peal there was a significant negative correlation between cough number and gastric pressure, but the slope for this relationship was very shallow, see figure 5 and table 1. Oesophageal pressures were not correlated with cough number (Table 1). Repeating the analysis using coughs 6 to 11, both gastric and oesophageal pressures significantly decreased with cough number. Combining all 11 coughs, gastric pressure exhibited an overall significant negative correlation with cough number whereas oesophageal pressure was uncorrelated.

7.2.3 Cough Sounds

There were moderate to good negative correlations for both sound parameters with increasing cough number in all cases (Table 1).

7.3 Relationships between Cough Parameters

7.3.1 Single voluntary coughs

Firstly, the correlations between EMG and sound were explored at fixed operating volumes allowing effort level to vary (Table 2). There were generally significant positive correlations between EMG parameters and the sound parameters for single coughs. Correlations tended to be stronger at the higher operating volumes, for the lateral chest and lateral abdominal muscles and when the AUC measures were used. Correlations between $sound_{MAX}$ and pressure were moderate overall but again stronger for higher operating volumes (Table 2). There were moderate to strong correlations between the EMG for all muscle groups and both pressure parameters, across all operating volumes studied (Table E1).

Secondly, the correlations between EMG and sound were explored at fixed effort levels allowing operating volume to vary (Table 3) and in contrast, there were few significant positive correlations, and these were extremely weak. There were moderate positive correlations between the EMG and both pressure parameters for all muscle groups across all efforts studied Table E2.

7.3.2 Voluntary Cough Peals

$Pgas_{MAX}$ correlated weakly with $sound_{MAX}$ in all cases however $Poes_{MAX}$ did not correlate with any sound parameter during cough peals Table 3. There were positive correlations between EMG parameters and the sound parameters for peal coughs in most cases and the correlations tended to be stronger for the AUC measures Table 3.
When all 11 peal coughs for all subjects were analysed $Pgas_{MAX}$ and EMG_{MAX} were moderately correlated for all muscle groups, regardless of the number of coughs used in the analysis, Table E2. $Poes_{MAX}$ however, did not meaningfully correlate with EMG_{MAX} during peal coughs Table E2.

8 DISCUSSION

This is the first study to investigate in detail the relative effects of effort and cough operating volume on respiratory muscle EMG, pressures in the chest and abdomen, and sound generated during both single voluntary coughs and voluntary cough peals. During single coughs, increasing effort produced substantial increases in all parameters measured, whereas the effect of operating volume was more complex. For single coughs EMG activity was inclined to increase at the extremes of volume whereas in cough peals, overall EMG measures decreased as the peal progressed and operating volume fell, however patterns between individuals were quite variable and in some cases EMG increased towards the end of the peal replicating findings in single low volume coughs. We also found cough sound parameters significantly but weakly correlated with both EMG and maximal pressures for single coughs and cough peals.

Few authors have previously investigated the volume of air inspired prior to cough (20, 21). Magni et al proposed from these studies, that for voluntary coughs the inspired volume relates to the anticipated forcefulness of the expulsive effort (22). Whilst this may be the case, we have demonstrated that in single coughs the effort applied has a greater effect than operating volume on cough EMG, pressures and sound. This can only be appreciated by controlling both cough effort and operating volume, allowing the impact of each and their interaction to be investigated.

Taking this approach, we found that coughs performed at operating volumes of 10% FVC (likely below FRC) had relatively higher EMG activity than those at higher operating volumes , perhaps because additional EMG activation is required to reach and then maintain a lung volume below FRC. Equally, at the extremes of lung volume, expiratory muscle length may not be optimal for coughing and therefore EMG activity is increased as a compensatory mechanism. Finally a change in orientation of the surface EMG electrodes as the operating volume changed could in part also explain some of the differences observed.

To our knowledge, this is the first study to also investigate EMG activity during voluntary cough peals, which typically occur in respiratory disease (23). However as the number of coughs between peals varied, choosing the most appropriate method of analysis to describe the changes as the peal progressed was challenging. We decided to first analyse up to the minimum number of coughs per peal (six), as this analysis included equivalent data from all subjects. We also repeated the analysis from the minimum coughs per peal to the median (eleven) and finally analysed all eleven peal coughs, however it must be noted that these subsequent analyses are less informative, as there is more missing data as a consequence of shorter cough peals.

Although it is difficult to make direct comparisons between single and peal coughs, it is possible to examine the changes in parameters as operating volume inevitably decreases for each cough in a cough peal, allowing some conclusions to be drawn. In the pooled data analysis, EMG activity appeared to overall reduce as the cough peals progressed, in contrast to increasing EMG for lower volume single coughs. However visual inspection of the individual peal data, in particular for very long cough peals (>15 coughs) did reveal that on some occasions EMG activity increased towards the end of the peal i.e. at low operating volumes (high cough number) as was the case for single coughs (Figure 6). This sort of variability probably explains the weak correlations between increasing cough number (reducing cough operating volume) and EMG parameters during a cough peal Table 2. Another possible reason for EMG activity differing between single cough and coughs peals is that effort may change as a cough peal progresses. We speculate that our data suggests that coughs early in a peal may require less effort to produce, hence coughing in peals may be adaptive and conserve energy however if coughing continues until the operating volume is below FRC, then effort conversely increases to maintain coughing. This may account for some of the differences between single coughs and cough peals seen in table 3; sound did not correlate with EMG for single coughs when effort was fixed whereas sound did correlate with EMG during cough peals.

Cough sound parameters better predicted cough effort than cough operating volume for single coughs and for cough peals decreased as the peal progressed, with $sound_{AUC}$ performing generally better than $sound_{MAX}$, however these correlations were generally weak. The behaviour of the $sound_{AUC}$ is compatible with a measure of flow. We could not confirm this as to measure cough flow simultaneously with cough sound requires the use of a mouthpiece or facemask, which would inevitably alter both the cough sound and the manner of coughing. One study has demonstrated even the use of a nose-clip influences cough sounds (24). Of note the correlations observed in this study significantly differ from a previous publication where cough sounds were studied when patients coughed into a facemask, additionally in that study participants were also trained to produce coughs which generated oesophageal pressures targeted within specific quintiles of maximum pressure, hence also somewhat artificial circumstances (15)

Currently, there is no accepted definition of cough intensity and although the perception of cough intensity is likely to include both social and psychological factors (4), the mechanical aspects of coughing are likely to feature highly. This study suggests that whilst cough sounds are related to the physiological processes during cough, the correlations observed in this study are overall weak and therefore sound is unlikely to be able to discriminate between coughs associated with greater EMG activity or pressure, parameters which are most likely to be important components of perceived cough intensity. Moreover, low operating volume coughs, whether single or at the end of a cough peal, have limited sound yet can be associated with the highest EMG activity observed.

This study had some limitations. Like others we have studied voluntary rather than spontaneous coughs and indeed this is necessary to control and study the effects of volume and effort. Also ECG contamination of the EMG signal is a well-known problem with EMG studies which we minimized by averaging over the ten coughs at each effort level and excluding the parasternal intercostal muscles.

In conclusion, we have shown for the first time that effort is a major determinant of voluntary cough EMG and that this effect is significantly modulated by the operating volume prior to coughing and future studies must take this into account. Notably, the cough sound amplitude and energy are related to the physiological changes during voluntary coughing but their potential utility as simple surrogate measures of cough intensity is limited.

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FIGURE LEGENDS

Figure 1: Illustration of EMG parameter calculations, data shown for a single voluntary cough. Parameters illustrated are maximum value (EMG_{MAX}) and the area under the curve (EMG_{AUC}).

Figure 2: EMG_{MAX} and EMG_{AUC} for coughs taken from operating volumes 10, 30, 60 and 90% of the subjects FVC. Data is plotted at fixed effort levels (low, medium and high) and presented as model means (upper/lower limits 95% confidence intervals). A p_{int} value <0.05 indicates that there is a significant interaction between cough effort and cough operating volume on EMG_{MAX} and $EMG_{AUC.}$

Figure 3: Maximum gastric and oesophageal pressures for coughs taken from operating volumes 10, 30, 60 and 90% of the subjects FVC. Data is plotted at fixed effort levels (low, medium and high) and presented as model means (upper/lower limits 95% confidence intervals). A p_{int} value <0.05 indicates a significant interaction effect between cough effort and cough operating volume

Figure 4: Sound parameters for coughs taken from operating volumes 10, 30, 60 and 90% FVC. Data is plotted at fixed effort levels (low, medium and high) and presented as model means (upper/lower limits 95% confidence intervals). A p_{int} value <0.05 indicates a significant interaction between cough effort and cough operating volume.

Figure 5: Model means for EMG, pressure and sound parameters for the first 6 peal coughs (estimated from GEE model). EMG plots are included for each muscle group studied.

Figure 6: EMG and gastric pressure and sound throughout a single cough peal. Data normalised to the parameter maximum within the cough peal. Data is from the first cough peal from one subject showing the relationship between muscle activation and gastric pressure for EMG_{MAX} (A), EMG_{AUC} (B) and sound.

Figure 1

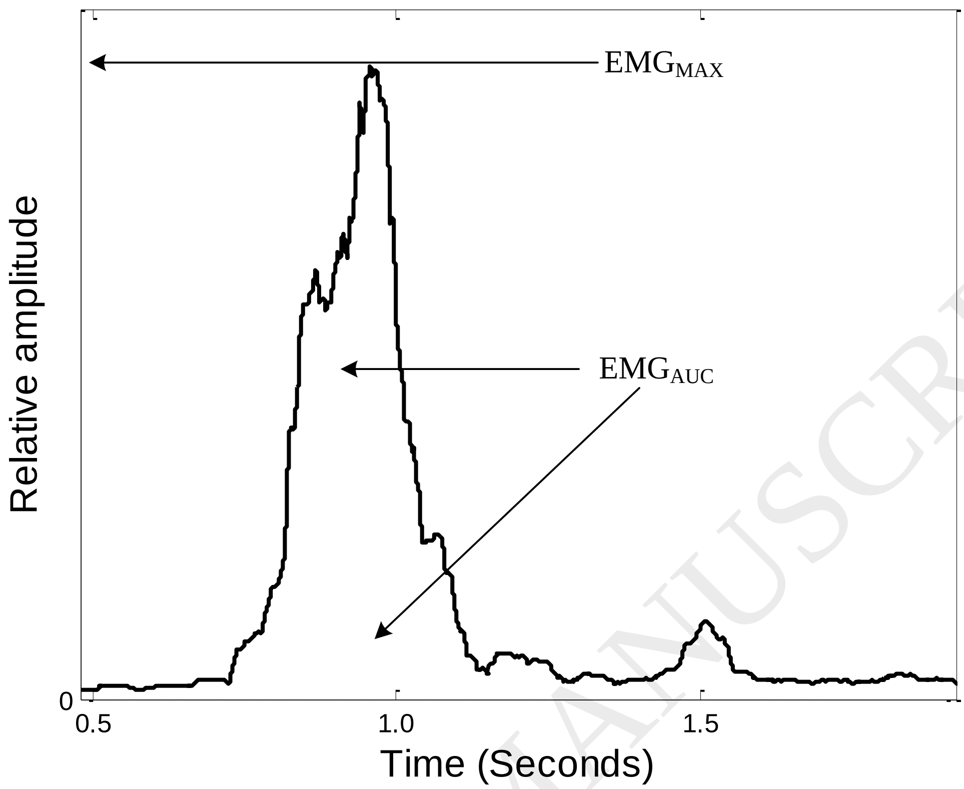


Figure 2

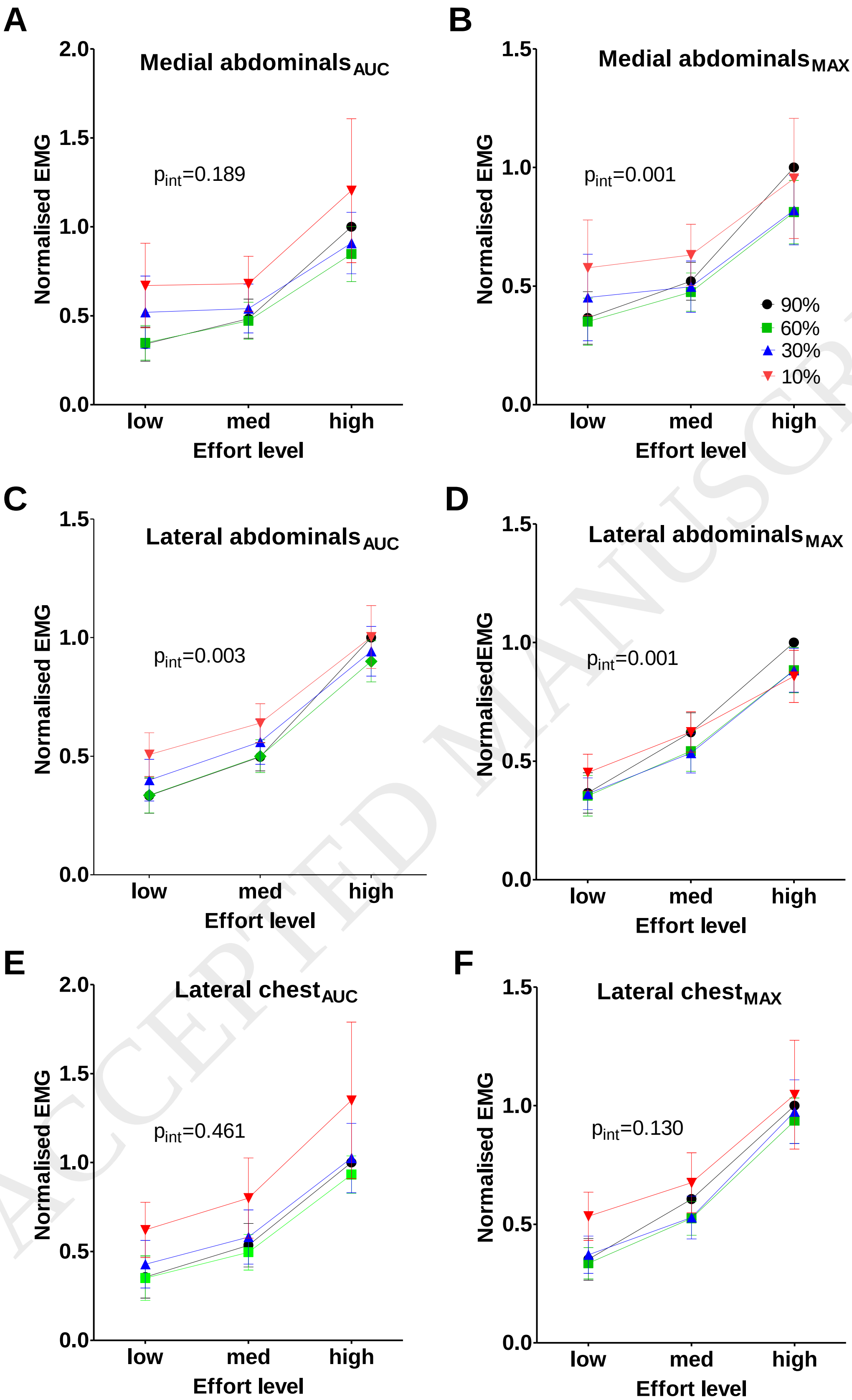

A
Medial abdominals AUC
pint=0.189
Normalised EMG
2.0
1.5
1.0
0.5
0.0
low
med
high
Effort level
B
Medial abdominals MAX
pint=0.001
Normalised EMG
1.5
1.0
0.5
0.0
90%
60%
30%
10%
low
med
high
Effort level
C
Lateral abdominals AUC
pint=0.003
Normalised EMG
1.5
1.0
0.5
0.0
low
med
high
Effort level
D
Lateral abdominals MAX
pint=0.001
NormalisedEMG
1.5
1.0
0.5
0.0
low
med
high
Effort level
E
Lateral chest AUC
pint=0.461
Normalised EMG
2.0
1.5
1.0
0.5
0.0
low
med
high
Effort level
F
Lateral chest MAX
pint=0.130
Normalised EMG
1.5
1.0
0.5
0.0
low
med
high
Effort level

Figure 3

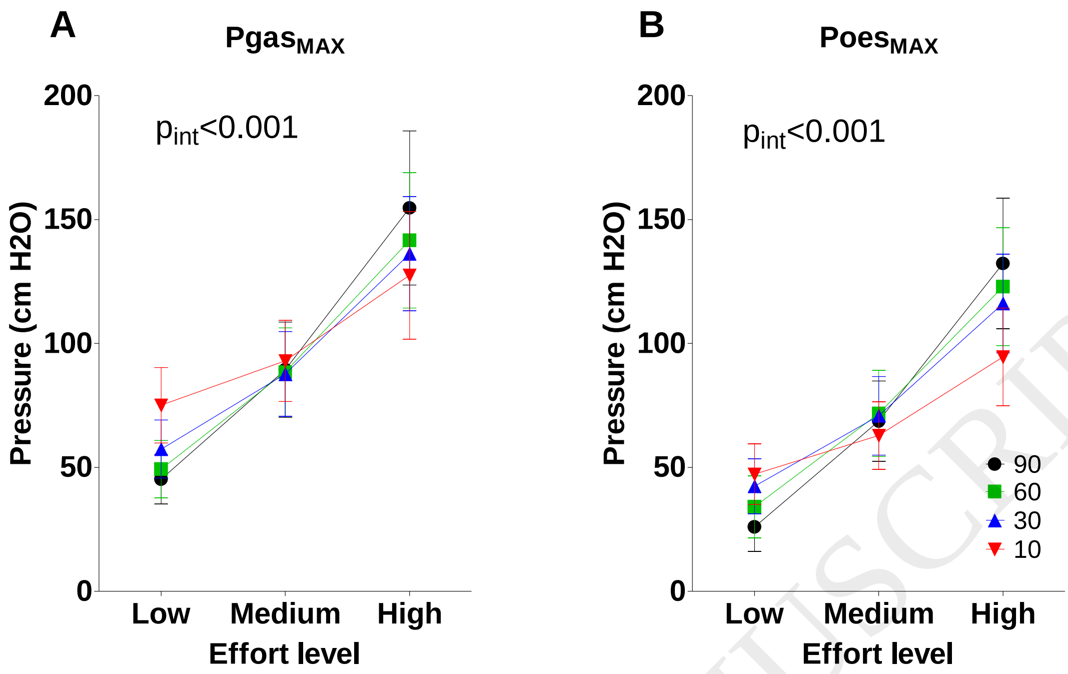

A
PgasMAX
200
150
100
50
0
Pressure (cm H2O)
pint<0.001
Low
Medium
High
Effort level
B
PoesMAX
200
150
100
50
0
Pressure (cm H2O)
pint<0.001
90
60
30
10
Low
Medium
High
Effort level

Figure 4

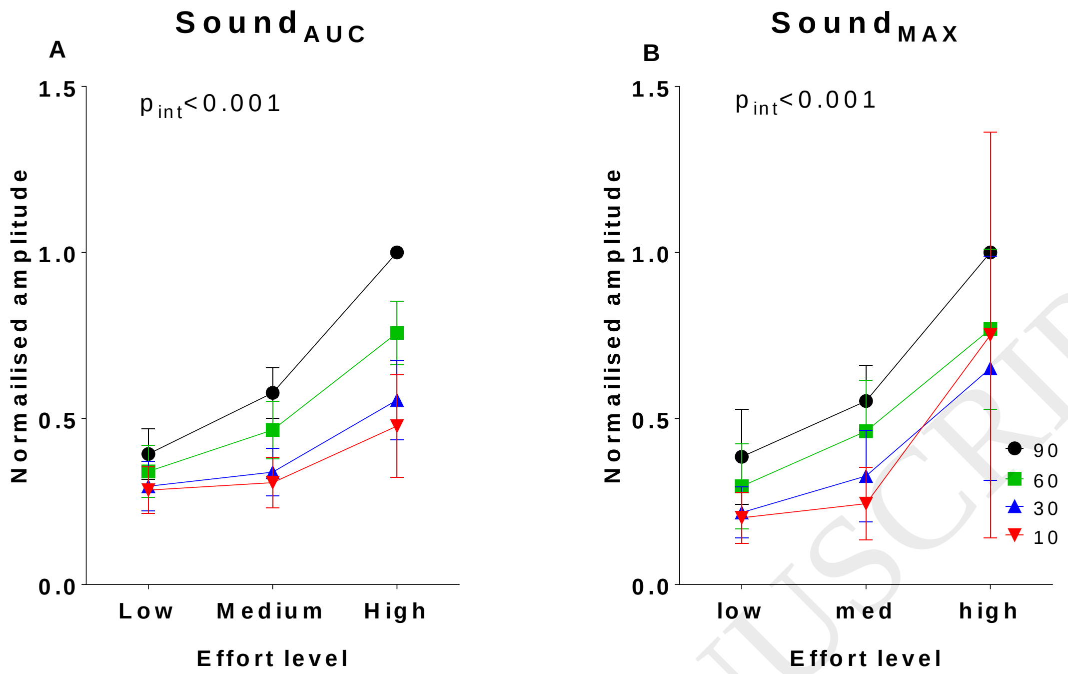

Sound AUC
A
1.5
1.0
0.5
0.0
p int<0.001
Normalised amplitude
Low
Medium
High
Effort level
Sound MAX
B
1.5
1.0
0.5
0.0
p int<0.001
Normalised amplitude
low
med
high
Effort level
90
60
30
10

Figure 5

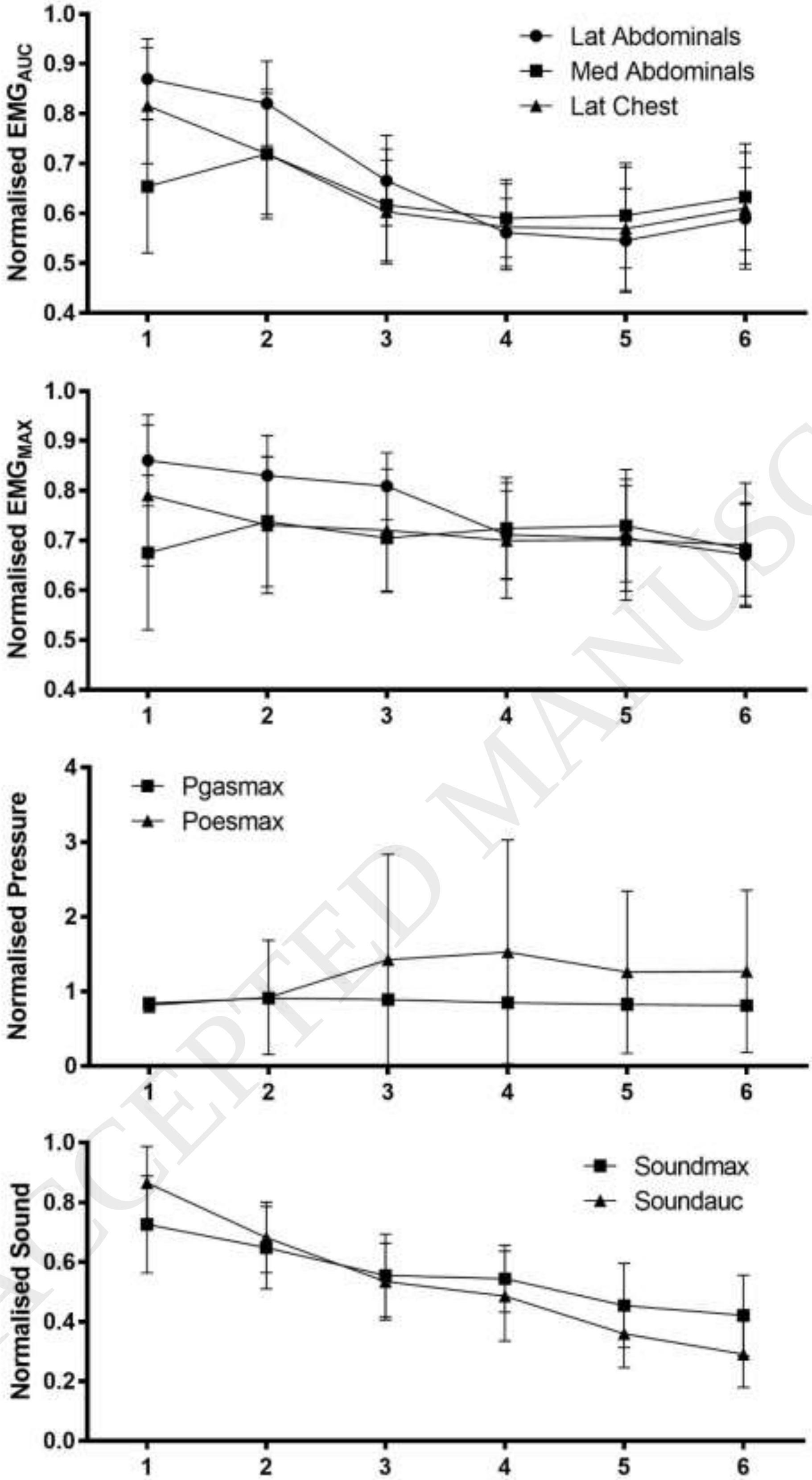
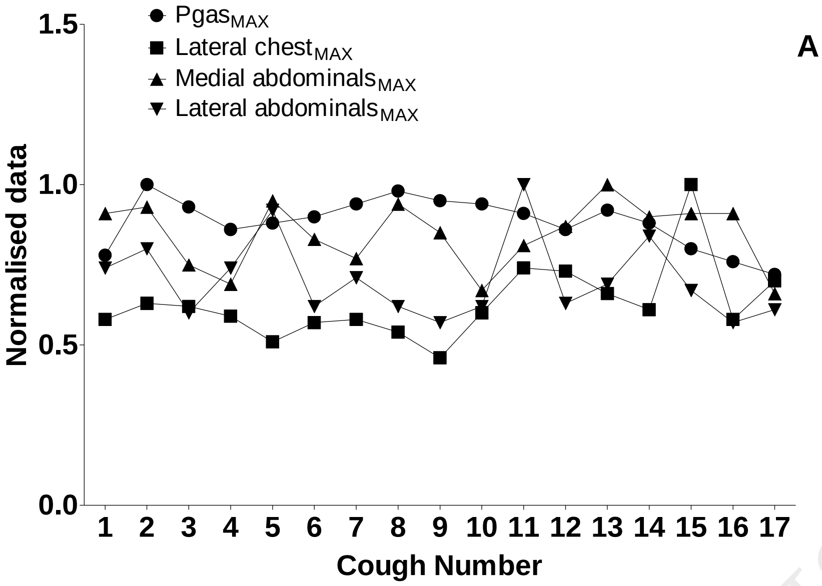

Lat Abdominals
Med Abdominals
Lat Chest
Normalised EMG$_{AUC}$
Normalised EMG$_{MAX}$
Pgasmax
Poesmax
Normalised Pressure
Soundmax
Soundauc
Normalised Sound
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.2
0.0
4
3
2
1
0
1
2
3
4
5
6

Figure 6


A
Pgas$_{MAX}$
Lateral chest$_{MAX}$
Medial abdominals$_{MAX}$
Lateral abdominals$_{MAX}$
Normalised data
1.5
1.0
0.5
0.0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
Cough Number

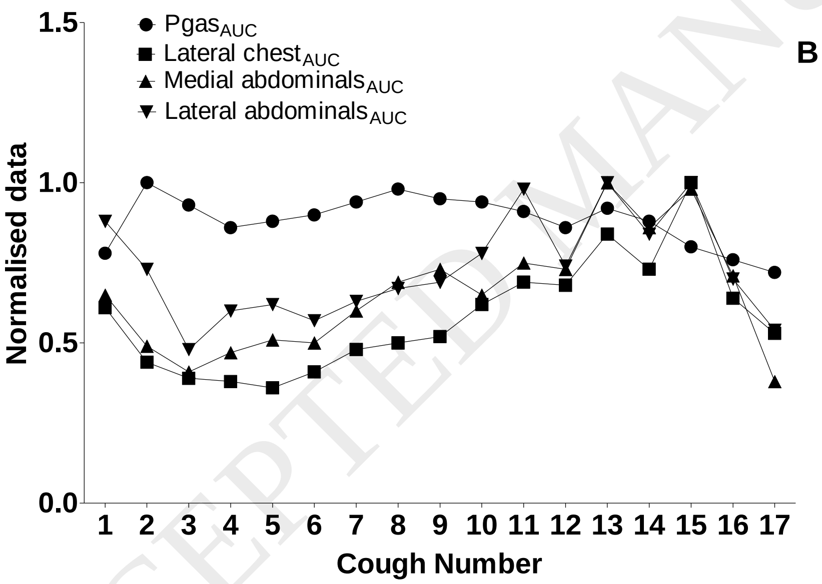

B
Pgas$_{AUC}$
Lateral chest$_{AUC}$
Medial abdominals$_{AUC}$
Lateral abdominals$_{AUC}$
Normalised data
1.5
1.0
0.5
0.0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
Cough Number

Table 1. Correlations between each parameter and cough number during cough peals. Data analysed including all peal coughs and during sections of cough peals. The first section includes coughs 1 to 6 (minimum number of coughs/peal) and the second section coughs 6 to 11 (median number of coughs/peal). Note this analysis includes all peals and an equivalent of number of coughs from each subject for section 1 but not section 2 or overall analyses. Data are presented as within-subject correlation coefficients (19).

Comparison		Peal coughs 1 (sectioned)								
		All coughs			Coughs 1 to 6			Coughs 6 to 11		
		r	P	Beta	r	p	beta	R	p	beta
Cough number	Lateral chest$_{MAX}$	**-0.429**	**<0.001**	**-0.024**	-0.225	0.06	-0.17	**-0.390**	**0.002**	**-0.035**
	Medial abdominal$_{MAX}$	**-0.211**	**0.017**	**-0.013**	0.008	0.947	0.001	**-0.315**	**0.015**	**-0.024**
	Lateral abdominal$_{MAX}$	**-0.551**	**<0.001**	**-0.035**	**-0.002**	**<0.001**	**-0.41**	**-0.299**	**0.021**	**-0.027**
	Lateral chest$_{AUC}$	**-0.316**	**<0.001**	**-0.018**	**-0.450**	**<0.001**	**-0.043**	-0.186	0.162	-0.016
	Medial abdominal$_{AUC}$	-0.148	0.094	-0.009	-0.152	0.206	-0.14	-0.180	0.173	-0.018
	Lateral abdominal$_{AUC}$	**-0.446**	**<0.001**	**-0.029**	**-0.609**	**<0.001**	**-0.066**	-0.125	0.345	-0.12
	Pgas$_{MAX}$	**-0.459**	**<0.001**	**-0.021**	**-0.237**	**0.047**	**-0.13**	**-0.427**	**0.001**	**-0.022**
	Poes$_{MAX}$	-0.042	0.637	-0.13	0.160	0.182	0.096	**-0.387**	**0.002**	**-0.146**
	Sound$_{MAX}$	**-0.543**	**<0.001**	**-0.049**	**-0.407**	**<0.001**	**-0.060**	**-0.463**	**<0.001**	**-0.043**
	Sound$_{AUC}$	**-0.757**	**<0.001**	**-0.07**	**-0.710**	**<0.001**	**-0.111**	**-0.496**	**<0.001**	**-0.025**

Table 2 Relationships between sound, pressure and EMG during single coughs taken from fixed operating volumes and varying effort and overall with both varying effort and operating volume. Data are presented as within subject correlation coefficients (19).

Comparison		Fixed operating volume (changing effort)								Overall	
		10% FVC		30% FVC		60% FVC		90% FVC			
		r	p	R	p	r	p	r	p	r	p
$Sound_{MAX}$	Lateral $chest_{MAX}$	**0.207**	**<0.001**	**0.431**	**<0.001**	**0.411**	**0.001**	**0.529**	**<0.001**	**0.277**	**<0.001**
	Medial $abdominal_{MAX}$	0.095	0.061	**0.166**	**0.001**	**0.383**	**<0.001**	**0.421**	**<0.001**	**0.171**	**<0.001**
	Lateral $abdominal_{MAX}$	**0.214**	**<0.001**	**0.377**	**<0.001**	**0.375**	**<0.001**	**0.525**	**<0.001**	**0.342**	**<0.001**
	$Pgas_{MAX}$	**0.281**	**<0.001**	**0.512**	**<0.001**	**0.487**	**<0.001**	**0.53**	**<0.001**	**0.352**	**<0.001**
	$Poes_{MAX}$	**0.296**	**<0.001**	**0.528**	**<0.001**	**0.528**	**<0.001**	**0.566**	**<0.001**	**0.39**	**<0.001**
$Sound_{AUC}$	Lateral $chest_{AUC}$	**0.338**	**<0.001**	**0.608**	**<0.001**	**0.637**	**<0.001**	**0.569**	**<0.001**	**0.364**	**<0.001**
	Medial $abdominal_{AUC}$	**0.126**	**0.013**	**0.201**	**<0.001**	**0.589**	**<0.001**	**0.579**	**<0.001**	**0.303**	**<0.001**
	Lateral $abdominal_{AUC}$	**0.39**	**<0.001**	**0.564**	**<0.001**	**0.642**	**<0.001**	**0.683**	**<0.001**	**0.511**	**<0.001**

Table 3. Relationships between sound, pressure and EMG during single coughs taken with fixed effort (varying operating volume) and during the same peal sections described for table 1, which inevitably include coughs taken from reducing operating volumes. Data are presented as within subject correlation coefficients and beta (19).

Comparisons		Peal coughs (changing operating volume)						Single coughs (changing operating volume)					
		Overall		Coughs 1 to 6		Coughs 6 to 11		low		Medium		High	
		r	p	r	p	r	p	r	p	r	p	r	p
$Sound_{MAX}$	Lateral $chest_{MAX}$	**0.454**	**<0.001**	0.383	**0.001**	**0.405**	**0.002**	**-0.094**	**0.028**	0	0.958	-0.008	0.854
	Medial $abdominal_{MAX}$	0.140	0.115	0.034	0.777	**0.319**	**0.014**	-0.024	0.572	-0.054	0.212	-0.008	0.845
	Lateral $abdominal_{MAX}$	**0.435**	**<0.001**	0.255	**0.032**	**0.267**	**0.041**	0.012	0.786	0.01	0.805	**0.137**	**<0.001**
	$Pgas_{MAX}$	**0.365**	**<0.001**	0.210	0.078	**0.416**	**0.001**	**-0.162**	**<0.001**	-0.058	0.186	0.033	0.44
	$Poes_{MAX}$	-0.094	0.290	-0.211	0.077	0.182	0.167	-0.013	0.748	0.076	0.08	**0.093**	**0.02**
$Sound_{AUC}$	Lateral $chest_{AUC}$	**0.484**	**<0.001**	**0.514**	**<0.001**	**0.324**	**0.001**	-0.06	0.144	-0.06	0.173	-0.044	0.308
	Medial $abdominal_{AUC}$	**0.316**	**<0.001**	**0.320**	**0.007**	**0.708**	**<0.001**	-0.058	0.172	-0.054	0.216	0.048	0.266
	Lateral $abdominal_{AUC}$	**0.607**	**<0.001**	**0.616**	**<0.001**	**0.458**	**<0.001**	-0.058	0.178	**-0.092**	**0.035**	**0.222**	**<0.001**